Attorney Docket No. 01662/53002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: M. Fleshner-Barak, et al.	Confirmation No. 7559
Application No.: 09/887,204	Art Unit: 1618
Filing Date: June 22, 2001	Examiner: FUBARA, Blessing M.

For: RAPIDLY EXPANDING COMPOSITION FOR GASTRIC RETENTION AND CONTROLLED RELEASE OF THERAPEUTIC AGENTS, AND DOSAGE FORMS INCLUDING THE COMPOSITION

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I hereby certify that this correspondence is being electronically deposited via EFS-Web to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on
Date: March 16, 2009
Signature: Fariza Juman
FARIZA JUMAN

DECLARATION UNDER 37 C.F.R. § 1.132

I, Vered ROSENBERGER, hereby declare and state as follows:

1. I am a co-inventor, along with Moshe FLESHNER-BARAK, E. Itzhak LERNER, Mazal DAHAN and Yisrael MAKOV, of the above-identified patent application, which has been assigned to Teva Pharmaceutical Industries Ltd. ("Teva"). I have 15 years of experience in the area of Drug Delivery Device Development and have been a Research and Development manager at Teva Pharmaceutical Industries, Ltd., since 2000. I received a Ph.D. in Biochemistry in 1993 from Tel-Aviv University. A copy of my CV is attached.

2. I have reviewed the Office Action mailed November 17, 2008, and the references cited therein, *i.e.*, U.S. patent No. 6,322,819 ("Burnside"), U.S. patent No. 4,326,525 ("Swanson"), and U.S. patent No. 5,874,090 ("Baker"). I have also reviewed pending claims 90-96 and 113-131.

4. I understand that the Examiner is of the opinion that Burnside discloses a multiple pulsed dose delivery system containing methylphenidate with a disintegration agent and a hydrogel and Swanson discloses a dosage form containing methylphenidate and tannic acid. According to the Examiner a combination of Burnside and Swanson would render the dosage forms claimed in the present application obvious.

5. I carried out experiments to determine the effect of the relative amounts of superdisintegrant, tannic acid, and hydrogel on the expansion and strength properties of gel formulations. These experiments were carried out in a manner similar to that described in the specification, e.g., Examples 1-3. The experimental results show that a gel formulation should contain superdisintegrant, tannic acid, and hydrogel in proportions (expressed as percentages) within the respectively recited ranges to have good expansion and strength suitable for use as a gastric retention vehicle. Table 1, below, presents experimental data on the effect of different percentages of tannic acid on the expansion and strength properties of gel formulations when the amount of superdisintegrant (croscarmellose sodium) was fixed at about 30%±2%. The amounts of hydrogel for these samples, *i.e.*, the total of Klucel and Methocel, were adjusted to make up the differences. The data in Table 1 show that optimal overall expansion and strength for these gels were achieved with about 4% to 8% tannic acid for gel formulations having about 30%±2% of superdisintegrant (croscarmellose sodium). The effect of the amounts of tannic acid on gel strength and expansion are also graphically illustrated in Figures 1 and 2. Table 2 presents experimental data on additional gel formulations. The data in Table 2 show that a gel formulation containing no tannic acid exhibited virtually no expansion. The data in Table 2 also show that the amount of tannic acid could be increased to about 10% if the amount of croscarmellose sodium was reduced to about 22%. With respect to the lower end of the recited range of tannic acid, it is my experience that when the amount of tannic acid is decreased to about 2%, a suitable gel can be obtained if the amount of the superdisintegrant is increased to higher than about 32%, and the relative amounts of Klucel and Methocel are adjusted.

Table 1

Ingredients		28/33	28/37 A	28/31C	28/32	28/34	28/40	28/41	28/42	28/43	28/44
Klucel HF		48	47.7	47.4	47.2	46.6	46.6	46.3	45.6	45	43.9
Croscarmellose Sodium		31.9	31.7	31.5	31.4	31	30.8	30.5	29.8	29.1	28.1
Methocel K15M		16	16	15.9	15.7	15.5	15.1	14.7	14.1	13.4	12.4
Tannic Acid		3.1	3.6	4.2	4.7	5.9	7	8	10	12	15
Magnesium Stearate		1	1	1	1	1	0.5	0.5	0.5	0.5	0.5
0.25H	Gel Size	21x15	soft	28x22	25x21	24x20	24x19	25x20	26x19	25x18	23x16
1H	Gel size	21x15	Fall apart	33x25	32x23	29x25	29x29	29x27	28x20	27x19	25x17
	Strength	120		26.5	51	90	147	125	130	120	121
	weight	2.5	NP	9.0	8.7	8.2	7.4	7.5	6.2	5.5	4.1
3H	Gel size	NP	NP	NP	NP	31x24	31x22	31x22	29x20	27x20	NP
	Strength	NP		Very soft		35	95	121	127	159	

The gel blend was compressed using an oval shape punch (17 mm length x 8.8mm). The initial gel weight range was 820-850mg.

Table 2

Ingredients		Ref	28/59*
Klucel HF		53.6	50.3%
Croscarmellose Sodium		25.3	22%
Methocel K15M		20.1	16.7%
Tannic Acid		0.0	10%
Magnesium Stearate		1.0	1.0
0.25H	Gel Size	18x10	23.5x18.7
1H	Gel size	18x11	27.2x20.9
	Strength		158
	weight	1.4	5.92
3H	Gel size		28.2x21.2
	Strength		157

*After 60min very smooth and strong gel

Figure 1: Effect of amount of tannic acid on strength of gel formulation

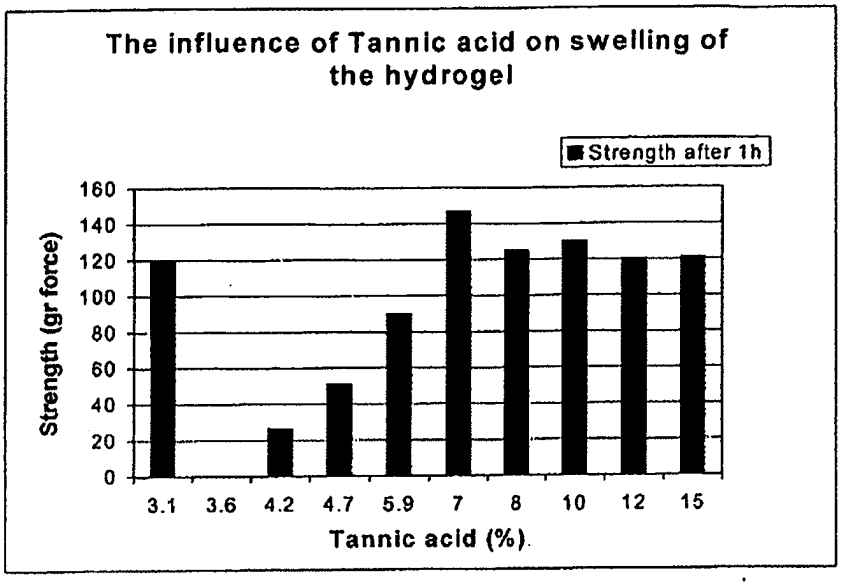
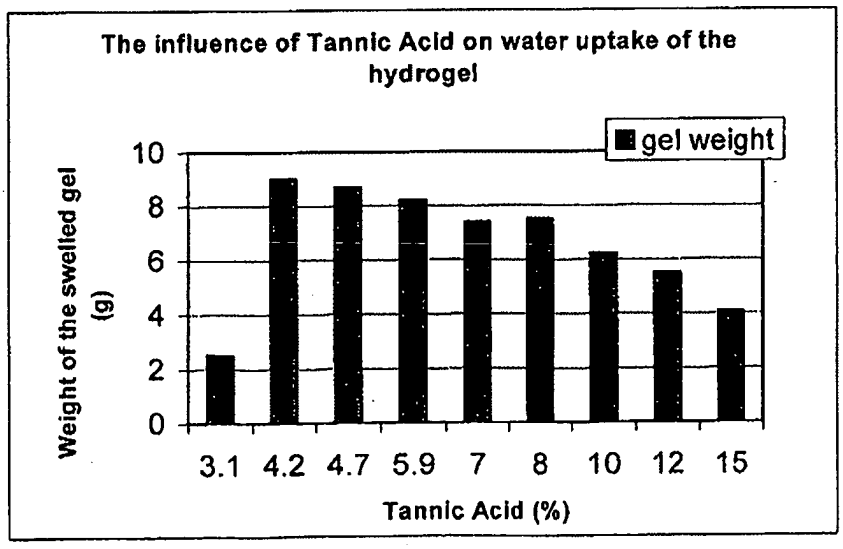


Figure 2: Effect of amount of tannic acid on expansion of gel formulation



6. Based on these experiments, it is my opinion that one of ordinary skill in the art would not have been led by Burnside and Swanson to the claimed compositions. The experimental data presented above demonstrate that to achieve expansion and strength suitable for use as a gastric retention vehicle, a gel formulation must contain superdisintegrant, tannic acid, and hydrogel in appropriate relative amounts, *i.e.*, in appropriate proportions. The effect of the relative amounts of superdisintegrant, tannic acid, and hydrogel on expansion and strength of gel formulations, and the recited ranges of the relative amounts of superdisintegrant, tannic acid, and hydrogel for achieving the expansion and strength suitable for use as a gastric retention vehicle, are not taught or suggested by, and could not have been predicted from, Burnside and Swanson.

I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that the undersigned acknowledges that any false statements and the like so made are punishable by fine or imprisonment or both under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of any patent that issues from the above-identified application.

Date: 9/3/09

Vered ROSENBERGER, Ph.D.